

## Surgical Management of Keratoconus

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## Financial Disclosure

- ♦ Jim Owen, OD has no financial interests in any of the products or companies discussed in this program

## Keratoconus



Asymmetric, bilateral progressive, thinning disorder of the cornea

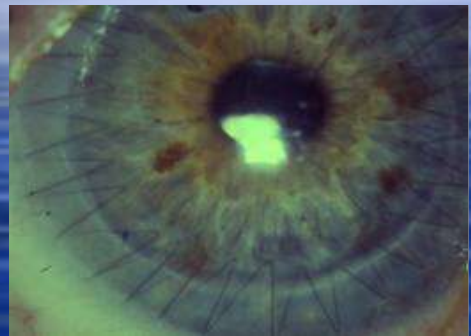
## Keratoconus

- ♦ Adolescent onset
- ♦ Progresses over 10-20 years
- ♦ Prevalence: 50-230/100,000<sup>1</sup>
- ♦ Incidence
  - ♦ 1/5000 in general population<sup>2</sup>
  - ♦ 2% in patients seeking surgical correction of refractive errors<sup>3</sup>
- ♦ About 10% of patients with KC require corneal transplantation

How Many PKP's Occur in the United States Secondary to Keratoconus?

- 1.500
- 2.2500
- 3.5000
- 4.7500

## Penetrating Keratoplasty



## Who is not at Risk



\*Malik et al., Biochem. Biophys. Acta, 1992  
 \*Seiler et al., Graefes Arch Clin Exp Ophthalmol 238:822, 2000  
 3 Spoerl et al., J Refractive Surg, 2009;24:7

## Percentage of Smokers and Nonsmokers in Average German Population and Patients With Keratoconus

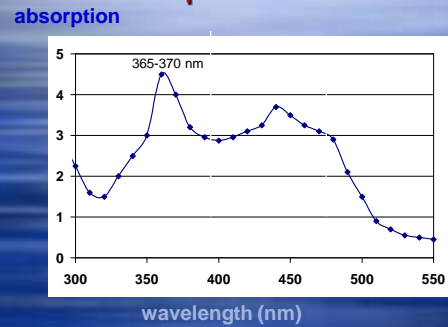
	Average Population	Keratoconus
Smokers	30	5
Non-Smokers	70	95

## Methods Of Stiffening the Cornea

- ♦ Glutaraldehyde crosslinking (prosthetic heart valves)
- ♦ Formaldehyde (pathology specimens)
- ♦ Aldehyde sugars (diabetes)
- ♦ UVA-induced crosslinking (dentistry)



## Riboflavin Absorption Spectrum



## Collagen Cross-Linking History

- ♦ Studied since 1994
- ♦ University of Dresden
  - ♦ Theo Seiler
  - ♦ Eberhard Spoerl
  - ♦ Gregory Wollensak



## III International Congress of Corneal Cross-linking

- ♦ Abbreviations in literature confusing
  - ♦ CCC
  - ♦ C3R
  - ♦ CCL
- ♦ Universal standard going forward - CXL



**Pachymetry**



**Riboflavin 0.1% q 2 minutes/30 minutes**



**Fluorescence in Anterior Chamber**



**Riboflavin q 2 minutes and UV Light for 30 minutes**



**UV Light for 30 Minutes**



**Bandage Contact Lens**



## Which step in this treatment gives you the most anxiety?

1. Removing epithelium
2. Applying Riboflavin
3. Exposing eye to UV Light
4. Applying Bandage Contact Lens
5. Watching Epithelium Grow

## Epithelial-On Crosslinking (Transepithelial CXL)

- ◆ First performed by Brian Boxer Wachler in 2004.
  - ◆ A few peer reviewed articles in medical literature
- ◆ Questions/concerns raised by Seiler and others:
  - ◆ Can enough riboflavin penetrate into the cornea?
    - ◆ Danger to endothelium & macula if too much UV enters the eye
    - ◆ Research: After 30 minutes:
      - ◆ Insufficient riboflavin concentration in the corneal stroma with Epi-On?
  - ◆ Does the Epithelium absorb too much UV:
    - ◆ This would diminish the effect of CXL?

William Trattler, MD

## Advantages of Epi-ON CXL

- ◆ Faster visual recovery:
  - ◆ Return to contact lenses in days
- ◆ Less pain
- ◆ Avoids risk of delays in epithelial healing
- ◆ Reduced risk of infection
- ◆ Reduced development of corneal haze



## CXLUSA

- ◆ Prospective Non-randomized Multicenter study evaluating:
  - ◆ Epi-On and Epi-Off CXL
    - ◆ Proprietary UV light Source
    - ◆ Age 10 and over

### Indications:

- Keratoconus
- FFKC
- Pellucid
- Post-LASIK ectasia

- Investigators:**
- Roy Rubinfield, Chevy Chase, MD
  - William Trattler, Charles Keiser, Carlos Bazzago, Miami, FL
  - Pang-Min Hsu, MD, Randy Epstein, MD, Chicago, IL
  - Lance Farnoff, Erik Larkson, Littleton, CO
  - David Wallace, Jonathan Davidorf, Los Angeles, CA
  - Sandy Feldman, San Diego, CA
  - Jodi Luchs, Long Island, NY
  - Jay Schwartz, Phoenix, AZ
  - Ty McCall, Brad Bowman, Henry Gellender, Dallas, TX
  - Dan Goodman, San Francisco, CA
  - John Talano, Kathryn Hatch, Boston, MA
  - Gregg Berdy, Ranjan Malhotra, Cleveland, OH
  - Bill Wiley, Shamm Rana, St. Louis, MO
  - John Hovanesian, Laguna Hills, CA
  - Audrey Talley Rostov, Seattle, WA
  - Mark Kontos, Spokane, W



## Keys to Trans-epithelial CXL

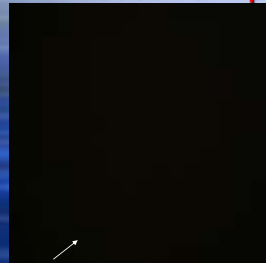
- ◆ Riboflavin 1% with gum cellulose Q2 min:
  - ◆ From local compounding pharmacies
- ◆ Topical Tetracaine with BAK provided Q2 to 5 min
- ◆ Corneal Protector sponge used
- ◆ 60-80 minutes of Riboflavin drops required



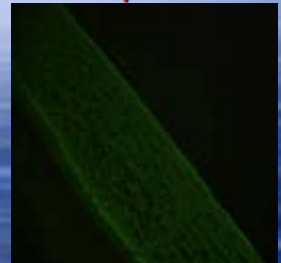
Corneal Protector sponge soaked with riboflavin

William Trattler, MD

## Fluorescence Microscopy 3000ms Exposure time, 10x



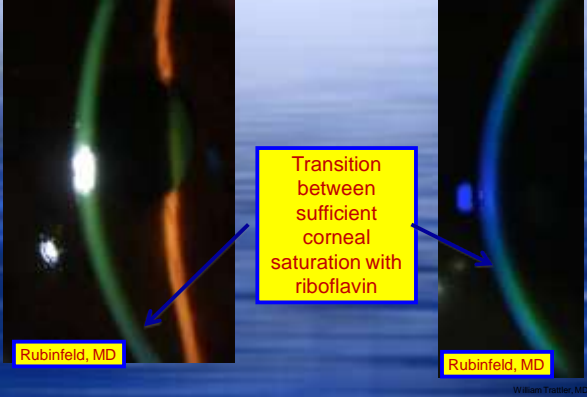
Riboflavin for 30 min,  
No UVA, with Epithelium



Riboflavin for 30 min,  
No UVA, no Epithelium

Asota, Fant, Edelhauser, and Stulting, unpublished

**Evaluation of Corneal Saturation: Epi-On**



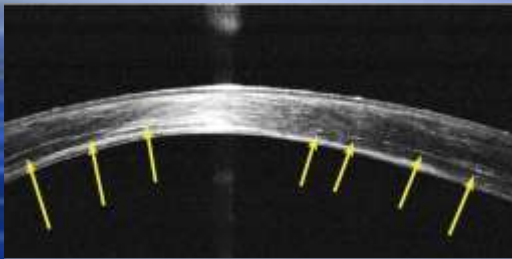
**Keys to Trans-epithelial CXL**

- ♦ 30 min of UV light applied:
  - ♦ Once sufficient riboflavin present in the corneal stroma
  - ♦ Minimum of 400 micron pach required before UV light



Fluorescence of cornea with UV light

**Optical Coherence Tomography**

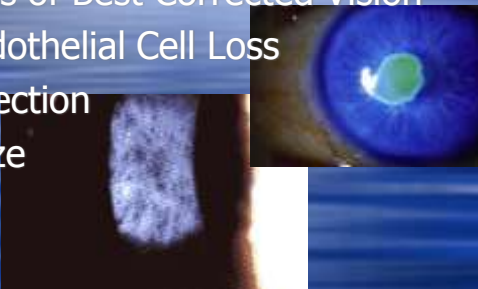


**Questions**

- Is it safe?
- Does it work?
- Who is a candidate?
- What is my role?

**Safety**

- ♦ Loss of Best Corrected Vision
- ♦ Endothelial Cell Loss
- ♦ Infection
- ♦ Haze



**Evaluation of Studies BCVA**

- ♦ Siena Eye Crosslinking Study
  - ♦ 44 Eyes followed 48 months
  - ♦ No loss of BCVA at 48 months
- ♦ Transepithelial Crosslinking Study
  - ♦ 55 Eyes followed 24 months
  - ♦ 1 patient 1 line decrease BCVA
  - ♦ 0 patients 2 line decrease BCVA

### Safety of corneal collagen cross-linking with UV-A and riboflavin in progressive keratoconus.

- ◆ No change in endothelial cell thickness at 6 months and 12 months
- ◆ No change in foveal thickness at 6 months and 12 months

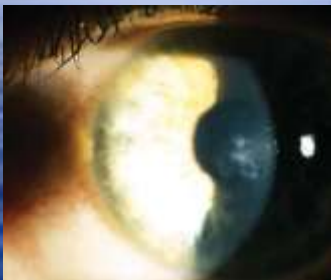
Cornea. 2010 Apr;29(4):409-11.  
 Safety of corneal collagen cross-linking with UV-A and riboflavin in progressive keratoconus.  
 Goldich Y, Marcovitch AL, Barkana Y, Avni I, Zadok D.

### Permanent Stromal Haze after Crosslinking

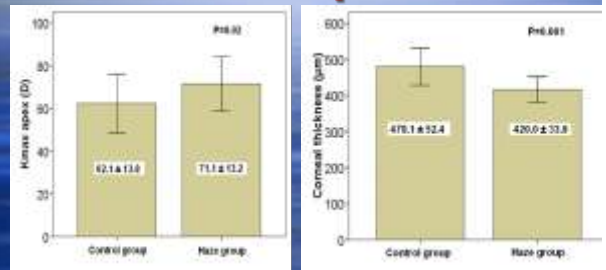
- ◆ 163 Eyes of 127 patients treated with Riboflavin and UV light (370nm)
- ◆ At 1 year 8.6% developed permanent stromal haze
- ◆ Study compared the clear group to haze group

Raiskup F. Permanent stromal haze after Riboflavin UV Crosslinking in Keratoconus  
 JRS; Sept 2009.

### Haze after CXL



### Differences in Haze Group

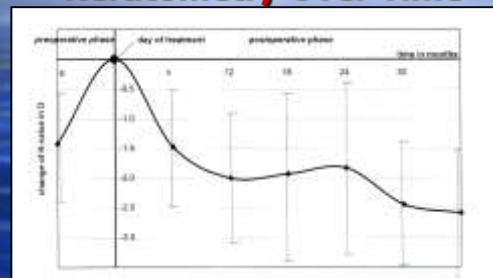


### Cross-Linking And Keratoconus

	Preoperative	Postoperative
No. of patients	22	
Mean follow-up	23.2 ± 12.9 mos	
Preoperative K progression	1.42 ± 1.18 D	
Postoperative K regression	2.01 ± 1.74	0.0001
Postoperative regression in SE	1.14 ± 2.18 D	0.030
Postoperative increase in VA	1.26 ± 1.5 lines	0.026

Wollensak, Spoerl, and Seiler, AJO 135:620, 2003.

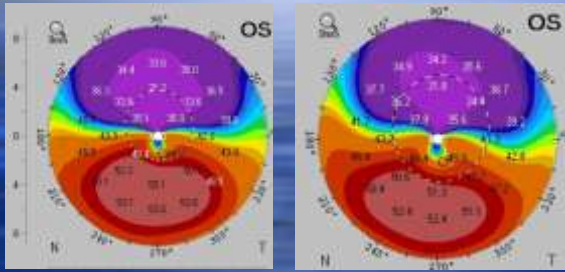
### Cross-Linking and Keratoconus Keratometry Over Time



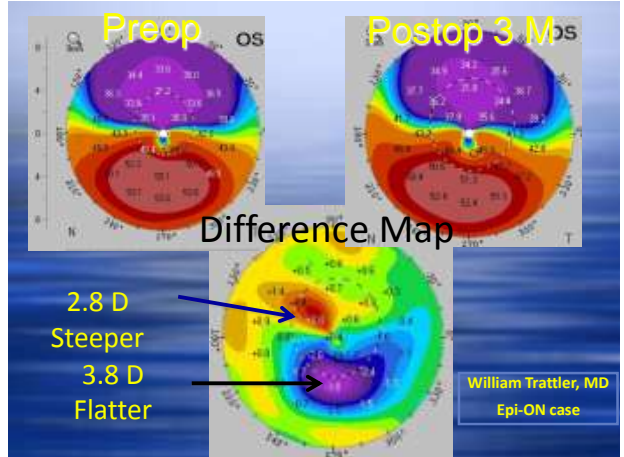
Wollensak, Spoerl, and Seiler, AJO 135:620, 2003.

## How Effective is CXL in this case?

Preop Postop 3 M



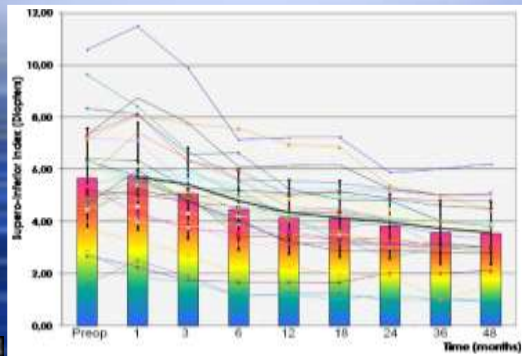
William Trattler, MD  
Epi-ON case



2.8 D Steeper  
3.8 D Flatter

William Trattler, MD  
Epi-ON case

## Topographic Symmetry



Source: *Journal of Ophthalmology* 2010; 149:405-409 (DOI:10.1016/j.joph.2009.10.021)  
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## Prospective Randomized Trial Design: Australia

- ◆ Christine Wittig, Grant Snibson, Mark Whiting, Laurie Sullivan, Richard Lindsay, Hugh Taylor
- ◆ Melbourne, Brisbane
- ◆ Inclusion criteria
  - ◆ Keratoconus
  - ◆ Documented progression over 12 mo.
  - ◆ CT > 400µ
  - ◆ Age 16-50
  - ◆ No corneal surgery or other pathology
- ◆ Cross-over at 6 months if progression in control eyes

## Prospective Randomized Trial Interim Results

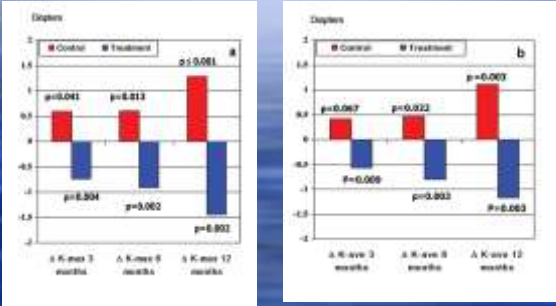
- ◆ 4/2006 – 11/2006
- ◆ 66 eyes randomized
- ◆ Mean age 27.6 y

## Prospective Randomized Trial Treatment Parameters

- ◆ Removal of epithelium
- ◆ Riboflavin drops q3 min x 15 min
- ◆ UVA with riboflavin q3 min
- ◆ Postoperative
  - ◆ TBL
  - ◆ Choramphenicol until ED healed
  - ◆ FML x 2 wk

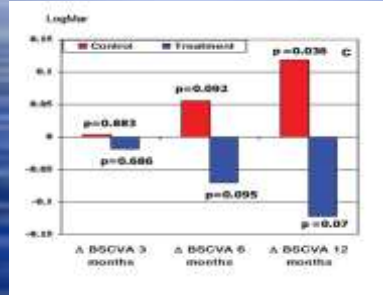


## Prospective Randomized Trial K<sub>max</sub> and K<sub>min</sub>



Wittig, A Randomized Control Trial of Corneal Crosslinking in Progressive Keratoconus; JRS Sept 2008

## Best Corrected Vision



## Long-term Results of Riboflavin UV A A Corneal Crosslinking for Keratoconus in Italy

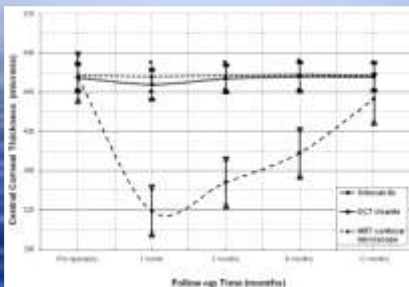
Aldo Caporossi, MD  
Cosimo Mazzatta, MD

American Journal of Ophthalmology  
Volume 149, Issue 4, Pages 585-593 (April 2010)  
DOI: 10.1016/j.ajo.2009.10.021

## Methods

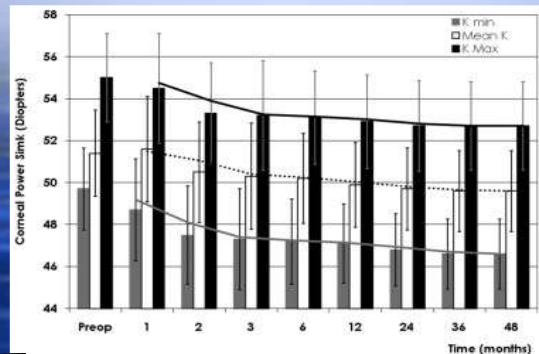
- ♦ 44 Eyes with progressive keratoconus
- ♦ Mean K less than 55
- ♦ Greater than 400 microns thickness
- ♦ Cornea clear without scars

## Corneal Thickness



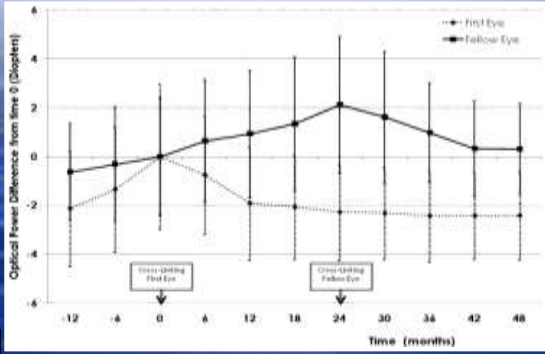
Source: [American Journal of Ophthalmology 2010, 149:585-593](#) (DOI: 10.1016/j.ajo.2009.10.021)  
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## Keratometry



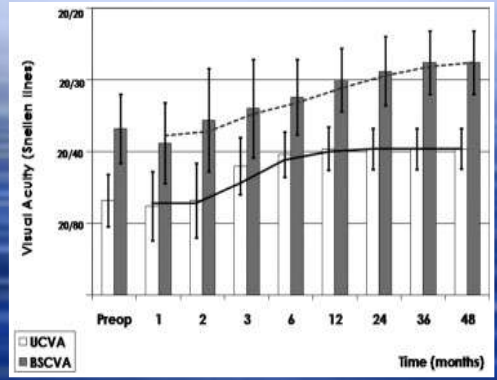
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### K Change as Compared to Fellow Eye



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### UCVA and BCVA



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### Comparison of Sequential vs Same-day Simultaneous Collagen Cross-linking and Topography-guided PRK for Treatment of Keratoconus

Anastasios John Kanellopoulos, MD

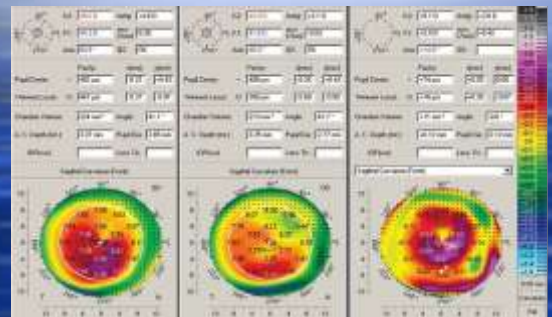
### Patient data and treatment

- ◆ 325 Keratoconus eyes
- ◆ Topography guided custom PRK
- ◆ CXL with riboflavin and UV light
- ◆ Maximum treatment 50 microns
- ◆ Treated 70% of cyl

### Results

- ◆ BCVA improved 0.39 logmar to 0.11
- ◆ 3.2 Diopter reduction in SE
- ◆ 3.5D Flatten of mean K's

### Pentacam Changes



Pre-op Post-op Difference

## What is the best parameter to measure success of CXL

1. Best Corrected Vision
2. Topographic Changes (I/S Ratio)
3. Change in Higher Order Aberrations
4. Patient Satisfaction Survey
5. Percentage of Soft Toric Wearers

## Conclusions : CXL

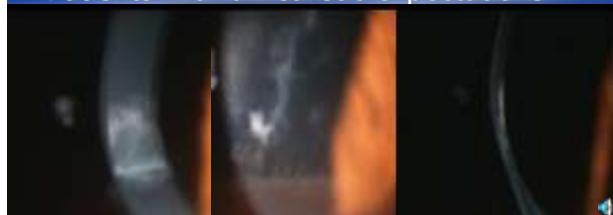
- ◆ Halts progression of ectatic corneal diseases
  - ◆ Decreases corneal curvature and thickness
  - ◆ Regularizes corneal surface
  - ◆ Improves UCVA and BSCVA
  - ◆ Effect lasts indefinitely
- ◆ Offers safe and effective treatment for conditions with no currently available treatment and may avoid
  - ◆ 15% of corneal transplants
  - ◆ Disability, cost, loss of productivity, CTL

## Indications for Intacs in Keratoconus or Post-Lasik Ectasia

- ◆ Patients are contact lens intolerant
- ◆ Are considering a cornea transplant
- ◆ Clear central cornea with no scar
- ◆ CL Visual acuity limits lifestyle
- ◆ Corneal thickness adequate at the site of proposed placement of segments

## Contra-indications for Intacs

- ◆ Cornea with central scars and opacities
- ◆ Cornea too thin at the site of the Intacs implantation
- ◆ Patients with unrealistic expectations



## Intacs with Sequential CXL

- ◆ Effects of both treatments are synergistic
  - ◆ Increased K flattening
  - ◆ Increased BCVA
  - ◆ Increased UCVA
- ◆ Kamburoglu G, Ertan A: Intacs Implantation with Sequential CXL Treatment in Postoperative LASIK Ectasia. *J Refractive Surg.* 2008;24:7:S726-S729
- ◆ Chan CC, Sharma M, Wachler BS: Effect of inferior-segment Intac with and without C3-R on keratoconus. *J Cataract Refract Surg.* 2007;33:75-80.



# Edema Post CXL / Intacs



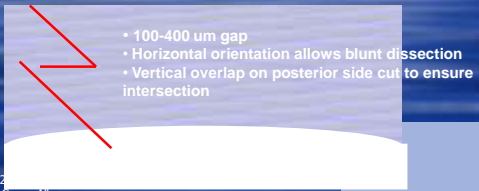
## Shapes



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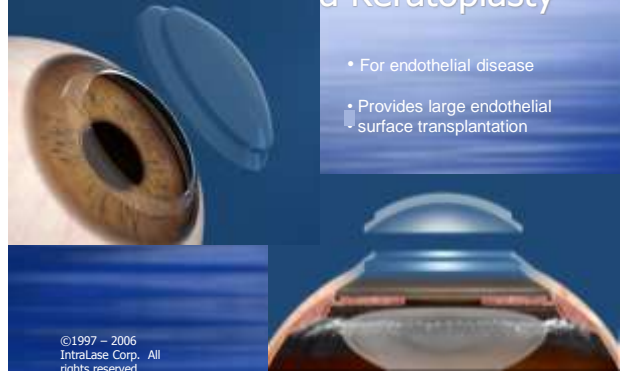
## Transition to Refractive Suite

- Just beginning
  - Interrupted cuts to preserve globe integrity
  - Donor tissue preparation
    - Collaboration with eye banks
  - Practical Mechanics



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## Top Hat Shaped Keratoplasty



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## Mushroom Shaped Keratoplasty



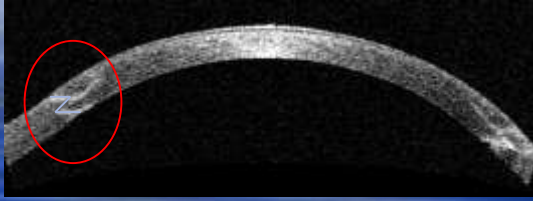
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## Zig-Zag Shaped Keratoplasty



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### Zig-Zag Shaped Keratoplasty



The Zig-Zag shaped incision creates a smooth corneal contour immediately after surgery with less distortion of the corneal optics and less astigmatism.

Image courtesy of Roger F. Steinert, MD  
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### IntraLase Advanced Keratoplasty



1 month OCT. The Zig-Zag shaped incision creates a smooth corneal contour immediately after surgery with less distortion of the corneal optics and less astigmatism.

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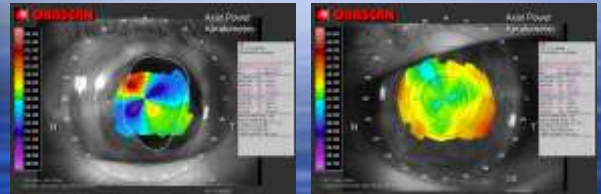
### IntraLase Advanced Keratoplasty



The Zig-Zag shaped incision is more prominent at 3 months, suggesting early fibrosis.

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### Zig-Zag Shaped Keratoplasty

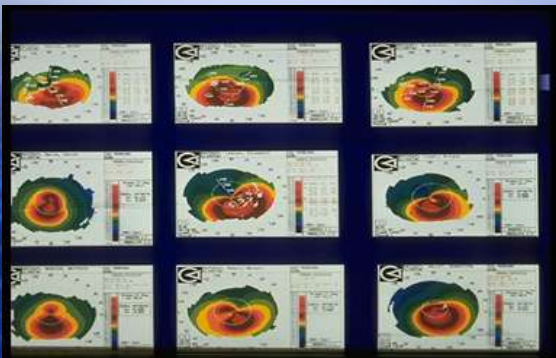


Trepine Cut Keratoplasty at 1 yr post-op result with **8 diopters of astigmatism**

IntraLase Enabled Keratoplasty at 3 months post-op result with **1/2 diopter of astigmatism**

Images courtesy of Roger F. Steinert, MD  
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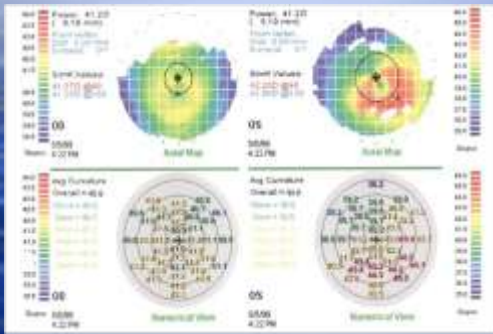
### Not all keratoconus is the same



### Case Study

- ◆ 38 y/o male
- ◆ OD – 3.00-1.25x135 20/25
- ◆ Soft toric never aligns to stable location
- ◆ Patient does not like comfort of RGP
- ◆ Vision with RGP 20/20-

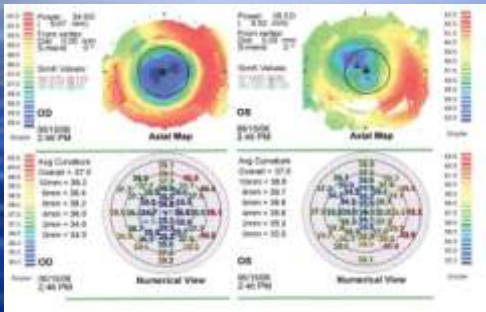
## Topography



## What is your recommended treatment?

1. SynergEyes
2. CXL
3. Intacs
4. CXL and Intacs
5. PRK

## Post – Op 10 years later



## Keratoconus Progression

- ♦ Early Keratoconus – Moves from Soft toric to RGP Lenses
- ♦ Advancing Keratoconus – RGP lenses to specialty RGP / Hybrid Lenses
  - ♦ Consider CXL / Intacs
- ♦ Advanced Keratoconus – Decreased wearing time
  - ♦ Intacs if stable
  - ♦ Intacs and CXL if not stable

Thank You

